REMARKS

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Initially, applicant would like to note that the present amendment is being submitted in compliance with "Amendments In A Revised Format Now Permitted", 1267 OG 4 (February 25, 2003). Pursuant to this notice, the requirements of 37 C.F.R. § 1.121 have been waived.

Applicant has amended the claims to cancel certain non-elected claims, except for those method or product claims that require the particulars of claim 1. Pursuant to the notice in the office action dated April 23, 2002, applicant requests rejoinder of claims 24-27 and 31, all of which require the particulars of claim 1, which is allowable for the reasons asserted below. Applicant has further introduced new claim 32, which depends from claim 1. Descriptive support for new claim 32 appears at page 10, lines 1-30.

The rejection of claims 1-5, 12, 13, and 20 under 35 U.S.C. § 112 (1st para.) for lack of enablement is respectfully traversed.

It is the position of the U.S. Patent & Trademark Office ("PTO") that the specification is not enabling for any antibodies other than the monoclonal antibody produced by the hybridoma CNCM-I-2476 disclosed in the present invention. The PTO cites U.S. Patent No. 5,773,572 to Fishleigh et al. ("Fishleigh") to support this position. In particular, the PTO cites to Fishleigh for using the same methods as those disclosed in the present application without apparent success in producing antibodies that recognize only the native disease specific form of PrP. While applicant does not dispute that Fishleigh fails to identify antibodies that recognize only the native disease specific form of PrP (i.e., when both isoforms are present in a sample in a native, non-denatured state), applicant respectfully disagrees that Fishleigh utilized the same methods and materials in preparing monoclonal antibodies.

Firstly, although Fishleigh teaches a polypeptide similar to that taught in the present invention for making the antibodies, it should be noted that the peptides of Fishleigh are not identical to those of the present invention (i.e., as recited in new claim 32). Furthermore, as noted in the present application, the peptide of SEQ ID No: 1 elicited a surprisingly strong immune response against PrP^{Sc}, which may be attributable to the

substitution of the Gln at position 207 with a Glu (page 10, lines 8-20). If a single amino acid substitution can make a significant difference in the antigeniticity of the peptide, it cannot be presumed that Fishleigh's peptides, which are similar but not identical to those of the present invention, should provide the same result as achieved in the present invention.

Secondly, Fishleigh does not set out using the same methods of antibody production as those disclosed in the present invention. In particular, the antibodies of Fishleigh are polyclonal, i.e., mouse antisera (col. 17, lines 38-41) or rabbit antisera (col. 19, lines 5-11), while those of the monoclonal antibody preparation of claim 1 are monoclonal antibodies or fragments thereof. It is known in the art that the antibody heterogeneity in a polyclonal antibody preparation often reduces its efficacy for *in vitro* uses, such as diagnostic applications (Kuby, J., "Hybridomas and Monoclonal Antibodies," Immunology Chap. 7, pg 141 Freeman & Co., New York (1992), which is attached hereto as Exhibit 1). The specification at page 1, teaches that monoclonal antibodies are preferable in the present invention for reasons of cross-reactivity. Applicant submits that one of skill in the art, having read Fishleigh, would have recognized that Fishleigh did not practice the invention of claim 1.

Finally, for substantially the same reasons as set forth in the response submitted in July 2002 (Paper No. 16), applicant submits that by reading and carrying out the present invention as disclosed, an individual skilled in the art would be fully able to make a monoclonal antibody preparation that includes monoclonal antibodies or fragments thereof capable of selectively binding to a three dimensional conformation provided by the C-terminal part of the PrP^{SC} isoform of the prion protein or a portion thereof, while not binding to the PrP^{C} isoform when both isoforms are present in a sample in a native, non-denatured state.

For all the foregoing reasons, applicant submits that the rejection of claims 1-5, 12, 13, and 20 for lack of enablement is improper and should be withdrawn.

The rejection of claims 1, 3-5, 13, and 20 under 35 CFR § 102(e) as anticipated by U.S. Patent No. 6,261,790 to O'Rourke ("O'Rourke") is respectfully traversed.

O'Rourke discloses monoclonal antibodies that specifically bind a conserved epitope of prion proteins, and the use of such antibodies to detect PrP^{Sc} in fixed or unfixed tissue that has been treated to unmask the PrP^{Sc} epitope and eliminate the availability of a corresponding epitope of PrP^{C} (see Abstract and Claim 1, col. 17). Due to the fact that PrP^{C} is less resistant to exogenous influences such as proteinase K treatment or, as used in

O'Rourke, heat treatment, only the PrP^{Sc} isoform survives the treatment and is detected with the antibody. The need for a denaturing treatment, such as applying heat to a sample prior to antibody detection, as required by O'Rourke, clearly shows that the antibody of O'Rourke is not capable of selectively distinguishing between the PrP^{C} and PrP^{Sc} isoforms in a sample without exogenous treatment. Thus, O'Rourke does not teach or suggest monoclonal antibodies or fragments thereof that are "capable of selectively binding to a three dimensional conformation provided by the C-terminal part of the PrP^{SC} isoform of the prion protein or a portion thereof, while not binding to the PrP^{C} isoform when both isoforms are present in a sample in a native, non-denatured state" (emphasis added), as presently recited in claim 1. Thus, O'Rourke fails to teach or suggest each and every limitation of the presently claimed invention.

For these reasons, the rejection of claims 1, 3-5, 13, and 20 under 35 CFR § 102(e) as anticipated by O'Rourke is improper and should be withdrawn.

The rejection of claims 1, 2, 4 ,5, 12, 13, and 20 under 35 CFR § 102(b) as anticipated by U.S. Patent No. 5,846,533 to Prusiner et al., ("Prusiner") is respectfully traversed in view of the above amendments.

Prusiner teaches antibodies that specifically bind to the non-denatured infectious prion protein PrP^{Sc} and can be used to assay a sample, which has any PrP^{C} denatured via proteinase K, for the presence of PrP^{Sc} of a specific species, which PrP^{Sc} is associated with disease. (See Prusiner Abstract).

The PTO cites col 35, lines 15-16, and Example 18 of Prusiner as evidence that Prusiner anticipates the invention of claim 1 by making antibodies that recognize the disease specific prion while not recognizing the cellular prion protein. Applicant respectfully disagrees. At col. 35, lines 15-16, Prusiner discusses the results of antibody testing that involved adding anti-PrP antibody to microtiter plate wells to which either PrP^{Sc} or PrP^{C} antigen was bound (but not both); and selecting for antibody which did not bind to the PrP^{C}-coated wells, but did bind when subsequently applied to the PrP^{Sc}–coated wells. The PTO also cites to Example 18, which shows the ability of various Fabs to immunoprecipitate a non-denatured SHaPrP 27-30, the infectious core of the prion protein. Applicant submits that in each of these examples, the antibody in question is reacted individually with either the PrP^{SC} isoform or the PrP^{C} isoform of the PrP antigen but not both. As a consequence, Prusiner fails to demonstrate exactly how the antibody would perform "when both isoforms are present in a sample in a native, non-denatured state" as presently recited in claim 1.

Furthermore, Prusiner fails to teach or suggest antibodies raised against a peptide having the amino acid sequence of either SEQ ID No: 1 or SEQ ID No: 2 (see new claim 32). Because Prusiner fails to teach the subject matter of new claim 32, this claim should likewise be allowable over Prusiner.

For all these reasons, the rejection of claims 1, 2, 4 ,5, 12, 13, and 20 under 35 CFR § 102(b) as anticipated by Prusiner is improper and should be withdrawn.

In view of all of the foregoing, applicant submits that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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